

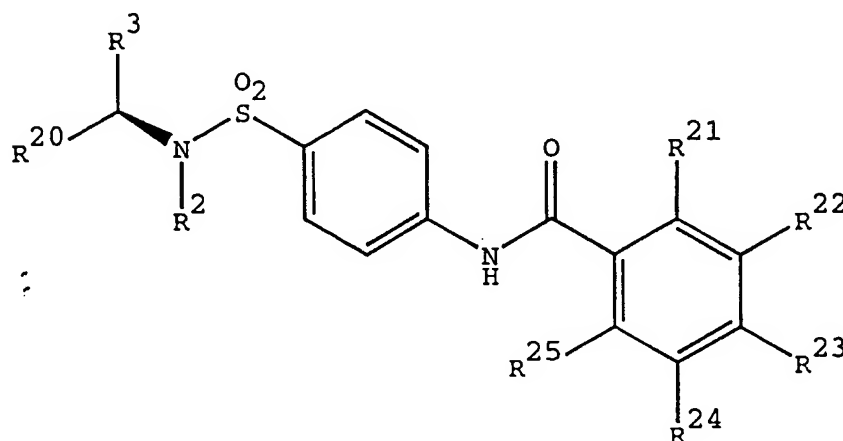
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CLAIMS

What is claimed is:

1. A matrix metalloproteinase inhibiting compound
5 having the structure:



10 or a salt, an enantiomer, a diastereomer, a
racemate, or a tautomer thereof, wherein:

R^2 is selected from the group consisting of H,
alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl,
alkylaryl, arylalkyl, alkoxyalkyl, hydroxyalkyl,
15 aminoalkyl, alkylaminoalkyl, heterocycloalkyl,
and heterocycloalkylalkyl;

R^3 is selected from the group consisting of H,
alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl,
alkylaryl, arylalkyl, alkoxy, alkoxyalkyl,
hydroxyalkyl, aminoalkyl, alkylaminoalkyl,
20 haloalkoxy, haloalkylthio, and heterocycloalkyl;

R^{20} is selected from the group consisting of
-C(O)OH, -C(O)NHOH, -SH, and -C(O)SH; and

R^{21} , R^{22} , R^{23} , R^{24} , and R^{25} are independently
selected from the group consisting of H, C_1 to
25 about C_{20} alkyl, C_1 to about C_{20} alkenyl, C_1 to
about C_{20} alkynyl, cycloalkyl, haloalkyl,
alkoxyalkyl, hydroxyalkyl, aminoalkyl,

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alkylaminoalkyl, nitroalkyl, heterocycloalkyl,
alkoxy, cycloalkoxy, alkoxycarbonyl,
alkoxyalkyl, haloalkoxy, haloalkylthio,
alkylamino, and carboxyalkyl.

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2. The matrix metalloproteinase inhibiting compound
of claim 1 wherein R^{20} is selected from the group
consisting of $-C(O)OH$ and $-C(O)NHOH$.

- 10 3. The matrix metalloproteinase inhibiting compound
of claim 2 wherein R^{21} and R^{25} are H.

4. The matrix metalloproteinase inhibiting compound
of claim 3 wherein R^{22} and R^{24} are H.

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5. The matrix metalloproteinase inhibiting compound
of claim 4 wherein R^{23} is C_1 to about C_{20} alkyl.

- 20 6. The matrix metalloproteinase inhibiting compound
of claim 5 wherein R^{23} is C_1 to about C_{20} linear
alkyl.

7. The matrix metalloproteinase inhibiting compound
of claim 2 wherein R^{20} is $-C(O)OH$.

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8. The matrix metalloproteinase inhibiting compound
of claim 7 wherein R^3 is selected from the group
consisting of alkyl, alkenyl, alkynyl,
haloalkoxy, haloalkylthio, and heterocycloalkyl.

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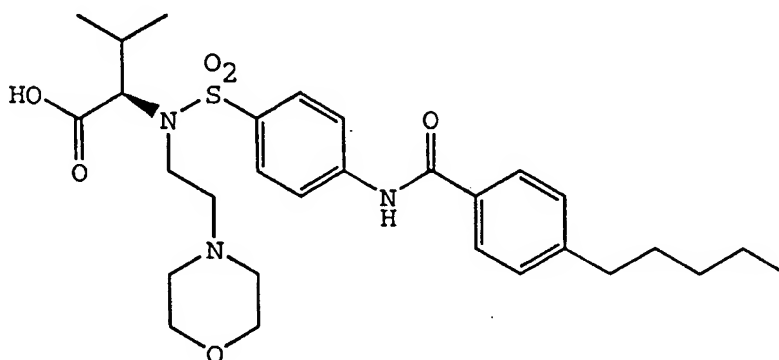
9. The matrix metalloproteinase inhibiting compound
of claim 8 wherein R^3 is heterocycloalkyl.

- 35 10. The matrix metalloproteinase inhibiting compound
of claim 9 wherein R^3 is 2-(N-morpholino)ethyl.

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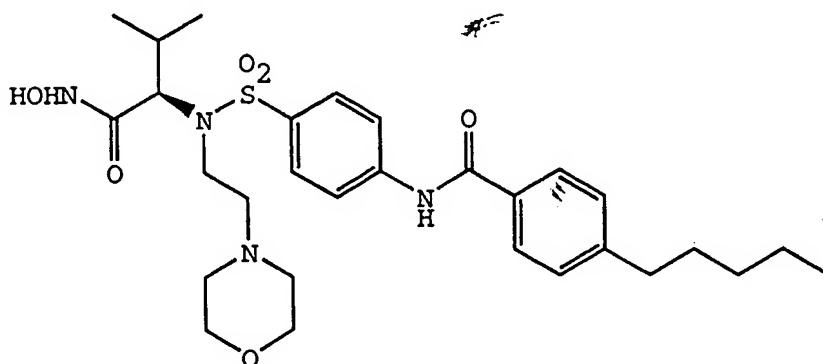
11. The matrix metalloproteinase inhibiting compound of claim 2 wherein R^{20} is $-C(O)NHOH$.
12. The matrix metalloproteinase inhibiting compound of claim 11 wherein R^3 is selected from the group consisting of alkyl, alkenyl, alkynyl, haloalkoxy, haloalkylthio, and heterocycloalkyl.
13. The matrix metalloproteinase inhibiting compound of claim 12 wherein R^3 is heterocycloalkyl.
14. The matrix metalloproteinase inhibiting compound of claim 13 wherein R^3 is 2-(N-morpholino)ethyl.
15. The matrix metalloproteinase inhibiting compound of claim 14 having the structure



- or a salt, an enantiomer, a racemate, or a tautomer thereof.
16. The matrix metalloproteinase inhibiting compound of claim 14 having the structure

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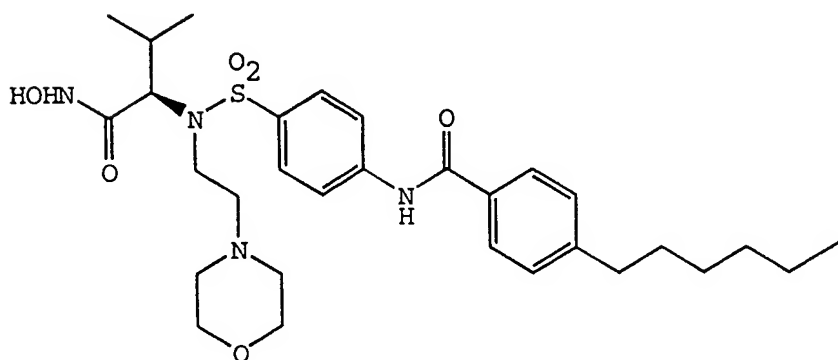
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or a salt, an enantiomer, a racemate, or a tautomer thereof.

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17. The matrix metalloproteinase inhibiting compound of claim 14 having the structure



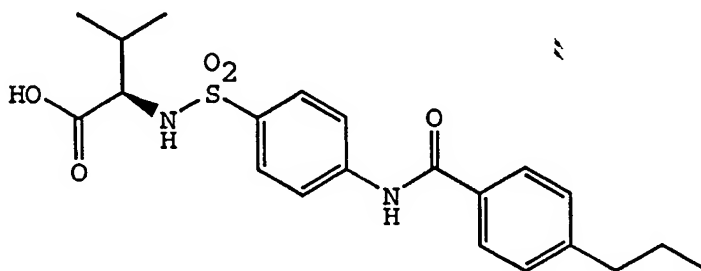
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or a salt, an enantiomer, a racemate, or a tautomer thereof.

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18. The matrix metalloproteinase-inhibiting compound of claim 14 having the structure

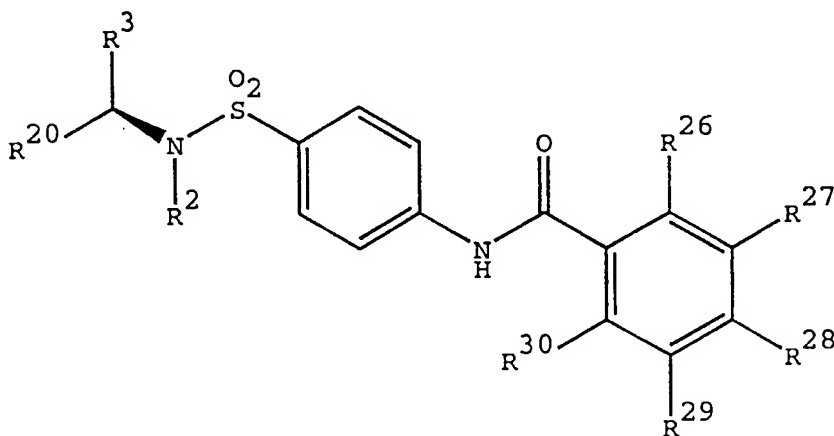


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or a salt, an enantiomer, a racemate, or a tautomer thereof.

19. A method of changing the conformation of a matrix metalloproteinase wherein the method comprises contacting the matrix metalloproteinase with a compound having the formula:

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or a salt, an enantiomer, a diastereomer, a racemate, or a tautomer thereof, thereby changing the conformation of the matrix metalloproteinase, wherein:

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R^2 is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl,

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alkylaryl, arylalkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, heterocycloalkyl, and heterocycloalkylalkyl;

5 R^3 is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl, alkylaryl, arylalkyl, alkoxy, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, haloalkoxy, haloalkylthio, and heterocycloalkyl;

10 R^{20} is selected from the group consisting of -C(O)OH, -C(O)NHOH, -SH, and -C(O)SH; and

R^{26} , R^{27} , R^{28} , R^{29} , and R^{30} are independently selected from the group consisting of about C_3 to about C_{20} alkyl, about C_3 to about C_{20} alkenyl, about C_3 to about C_{20} alkynyl, cycloalkyl, 15 haloalkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, nitroalkyl, heterocycloalkyl, alkoxy, cycloalkoxy, alkoxycarbonyl, alkoxyalkyl, haloalkoxy, haloalkylthio, alkylamino, and carboxyalkyl.

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20. The method of claim 19 wherein R^{20} is selected from the group consisting of -C(O)OH and -C(O)NHOH.

25 21. The method of claim 19 wherein R^3 is selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkoxy, haloalkylthio, and heterocycloalkyl

30 22. The method of claim 21 wherein R^3 is a C_1 to about C_{12} alkyl.

23. The method of claim 22 wherein R^3 is a C_1 to about C_4 alkyl.

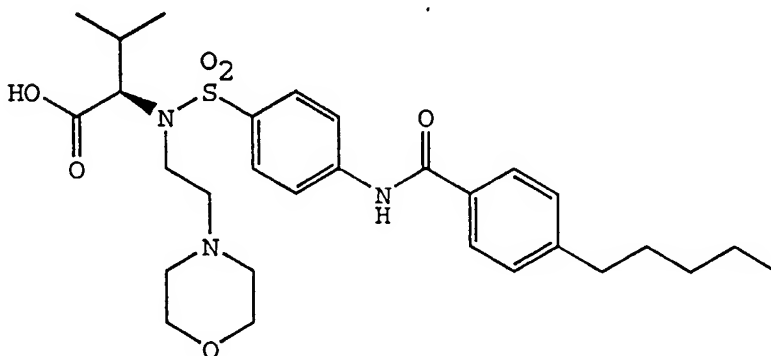
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24. The method of claim 23 wherein R^3 is isopropyl.

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25. The method of claim 19 wherein R^2 is heterocycloalkylalkyl.
- 5 26. The method of claim 25 wherein R^3 is 2-(N-morpholino)ethyl.
27. The method of claim 19 wherein R^{26} and R^{30} are H.
- 10 28. The method of claim 27 wherein R^{27} and R^{29} are H.
29. The method of claim 28 wherein R^{28} is about C_3 to about C_{20} alkyl.
- 15 30. The method of claim 29 wherein R^{28} is about C_3 to about C_{20} linear alkyl.
31. The method of claim 30 wherein R^{28} is selected from the group consisting of n-propyl, n-butyl, 20 n-pentyl and n-hexyl.
32. The method of claim 31 wherein the compound has the structure:

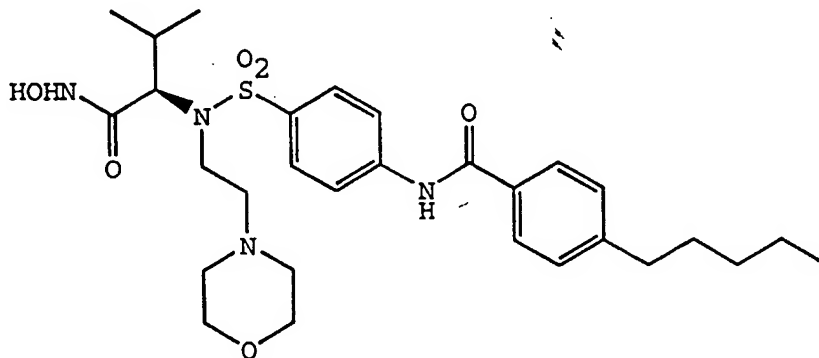


or a salt, an enantiomer, a racemate, or a tautomer thereof.

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33. The method of claim 31 wherein the compound has the structure:

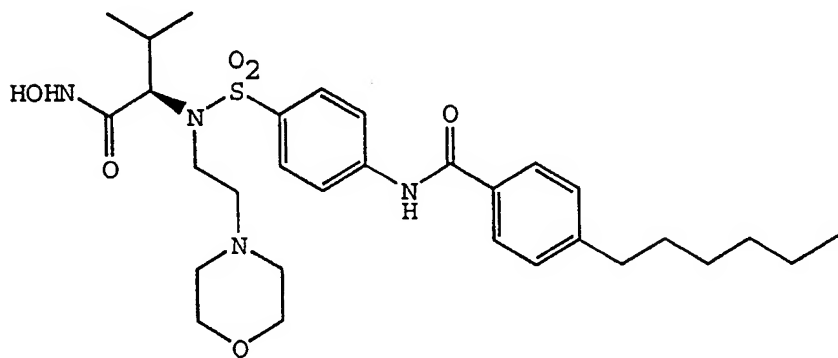


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or a salt, an enantiomer, a racemate, or a tautomer thereof.

34. The method of claim 31 wherein the compound has the structure:

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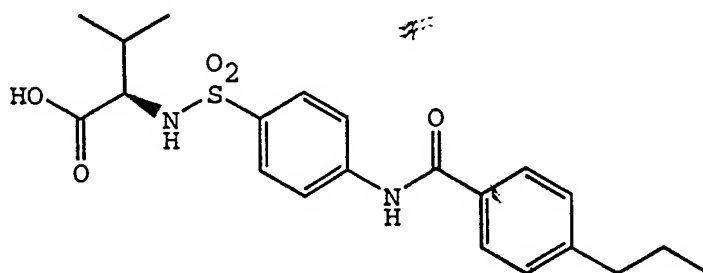
or a salt, an enantiomer, a racemate, or a tautomer thereof.

35. The method of claim 31 wherein the compound has the structure:

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or a salt, an enantiomer, a racemate, or a tautomer thereof.

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36. The method of claim 19 wherein the matrix metalloproteinase is selected from the group consisting of MMP-8 and MMP-13.

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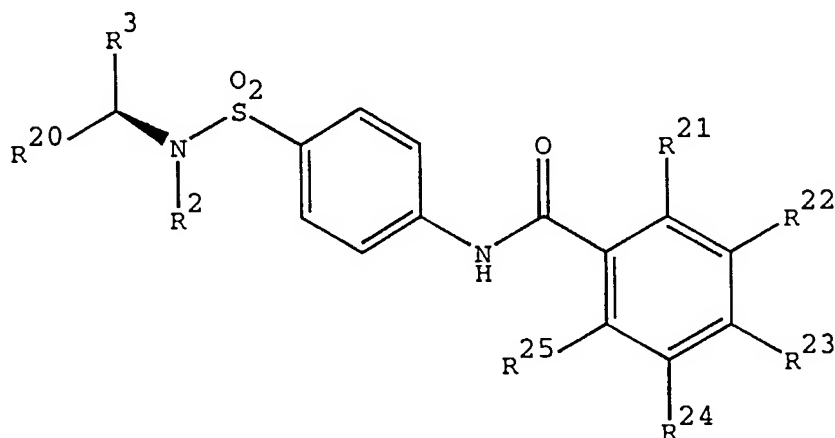
37. The method of claim 36 wherein the matrix metalloproteinase is MMP-8.

38. The method of claim 36 wherein the matrix metalloproteinase is MMP-13.

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39. A method of inhibiting a matrix metalloproteinase wherein the method comprises contacting the matrix metalloproteinase with a compound having the formula:

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or a salt, an enantiomer, a diastereomer, a
racemate, or a tautomer thereof, thereby
inhibiting the matrix metalloproteinase,
5 wherein:

R^2 is selected from the group consisting of H,
alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl,
alkylaryl, arylalkyl, alkoxyalkyl, hydroxyalkyl,
aminoalkyl, alkylaminoalkyl, heterocycloalkyl,
10 and heterocycloalkylalkyl;

R^3 is selected from the group consisting of H,
alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl,
alkylaryl, arylalkyl, alkoxy, alkoxyalkyl,
hydroxyalkyl, aminoalkyl, alkylaminoalkyl,
15 haloalkoxy, haloalkylthio, and heterocycloalkyl;

R^{20} is selected from the group consisting of
-C(O)OH, -C(O)NHOH, -SH, and -C(O)SH; and

R^{21} , R^{22} , R^{23} , R^{24} , and R^{25} are independently
selected from the group consisting of H, C_1 to
20 about C_{20} alkyl, C_1 to about C_{20} alkenyl, C_1 to
about C_{20} alkynyl, cycloalkyl, haloalkyl,
alkoxyalkyl, hydroxyalkyl, aminoalkyl,
alkylaminoalkyl, nitroalkyl, heterocycloalkyl,
alkoxy, cycloalkoxy, alkoxycarbonyl,
25 alkoxyalkyl, haloalkoxy, haloalkylthio,
alkylamino, and carboxyalkyl.

40. The method of claim 39 wherein R^{20} is selected
from the group consisting of -C(O)OH and
30 -C(O)NHOH.

41. The method of claim 39 wherein R^3 is selected
from the group consisting of H, alkyl, alkenyl,
alkynyl, haloalkoxy, haloalkylthio, and
35 heterocycloalkyl.

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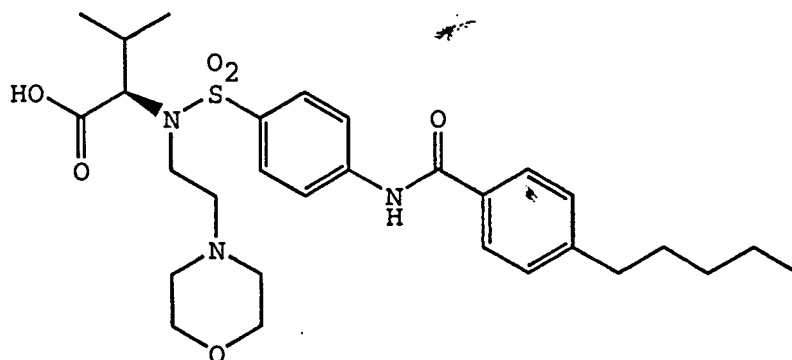
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42. The method of claim 41 wherein R^3 is a C_1 to
about C_{12} alkyl.
43. The method of claim 42 wherein R^3 is a C_1 to
5 about C_4 alkyl.
44. The method of claim 43 wherein R^3 is isopropyl.
45. The method of claim 39 wherein R^2 is
10 heterocycloalkylalkyl.
46. The method of claim 45 wherein R^2 is 2-(N-
morpholino)ethyl.
- 15 47. The method of claim 39 wherein R^{21} and R^{25} are H.
48. The method of claim 47 wherein R^{22} and R^{24} are H.
49. The method of claim 48 wherein R^{23} is C_1 to about
20 C_{20} alkyl.
50. The method of claim 49 wherein R^{23} is methyl or
 C_2 to about C_{20} linear alkyl.
- 25 51. The method of claim 50 wherein R^{23} is n-pentyl or
n-hexyl.
52. The method of claim 51 wherein the compound has
the structure:

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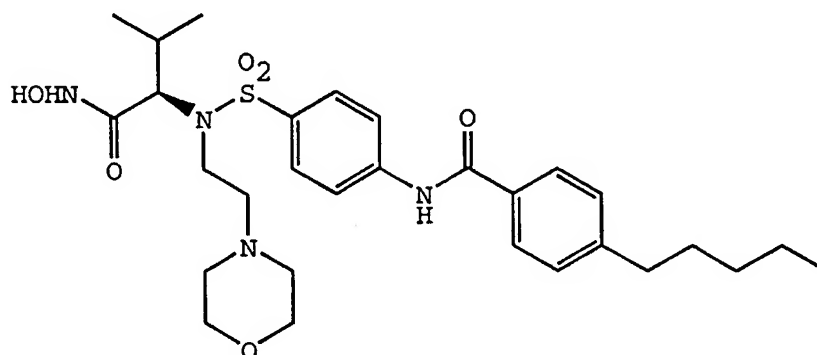
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or a salt, an enantiomer, a racemate, or a tautomer thereof.

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53. The method of claim 51 wherein the compound has the structure:



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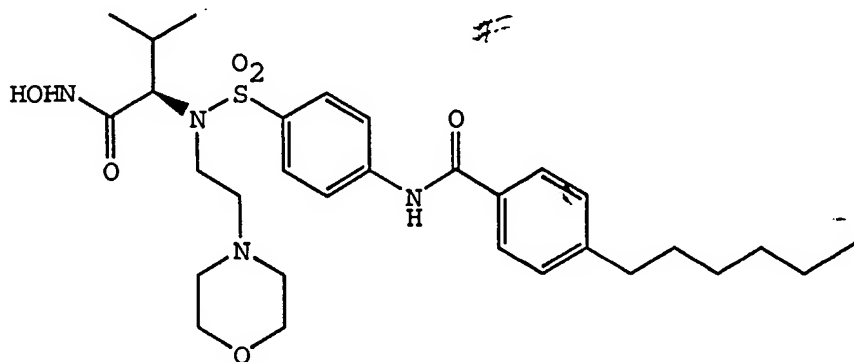
or a salt, an enantiomer, a racemate, or a tautomer thereof.

54. The method of claim 51 wherein the compound has the structure:

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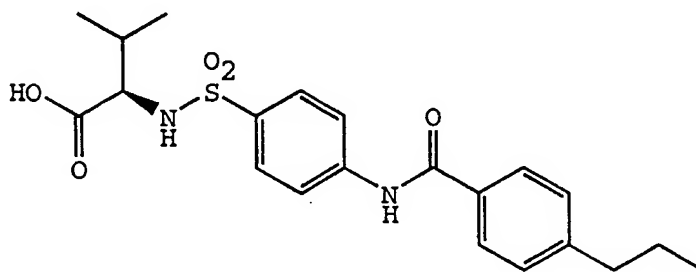
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or a salt, an enantiomer, a racemate, or a
tautomer thereof.

55. The method of claim 51 wherein the compound has
the structure:



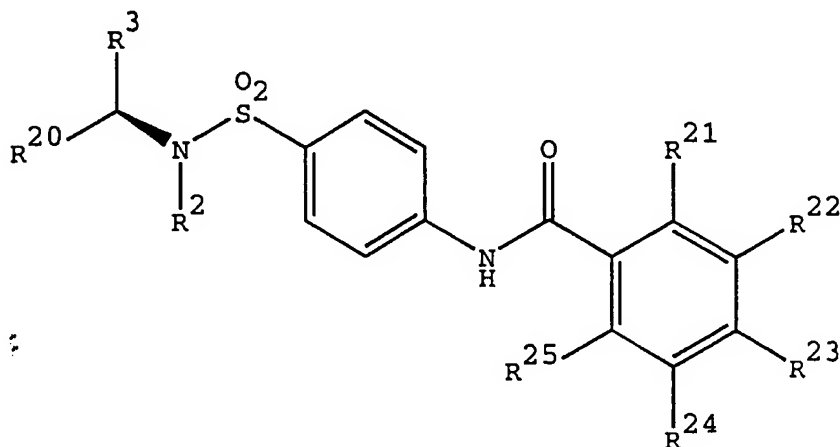
or a salt, an enantiomer, a racemate, or a
tautomer thereof.

56. The method of claim 39 wherein the matrix
metalloproteinase is selected from the group
consisting of MMP-8 and MMP-13.
57. The method of claim 56 wherein the matrix
metalloproteinase is MMP-8.
58. The method of claim 56 wherein the matrix
metalloproteinase is MMP-13.

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59. A method treating osteoarthritis in a mammal wherein the method comprises providing to the mammal an osteoarthritis-treating-effective amount of a compound having the formula:



or an enantiomer, diastereomer, racemate, or tautomer thereof, thereby treating osteoarthritis, wherein:

R^2 is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl, alkylaryl, arylalkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, heterocycloalkyl, and heterocycloalkylalkyl;

R^3 is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl, alkylaryl, arylalkyl, alkoxy, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, haloalkoxy, haloalkylthio, and heterocycloalkyl;

R^{20} is selected from the group consisting of $-C(O)OH$, $-C(O)NHOH$, $-SH$, and $-C(O)SH$; and

R^{21} , R^{22} , R^{23} , R^{24} , and R^{25} are independently selected from the group consisting of H, C_1 to about C_{20} alkyl, C_1 to about C_{20} alkenyl, C_1 to about C_{20} alkynyl, cycloalkyl, haloalkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl,

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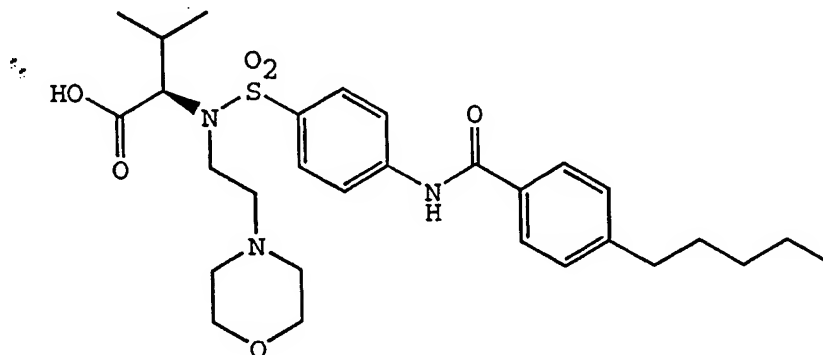
alkylaminoalkyl, nitroalkyl, heterocycloalkyl,
alkoxy, cycloalkoxy, alkoxycarbonyl,
alkoxyalkyl, haloalkoxy, haloalkylthio,
alkylamino, and carboxyalkyl.

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60. The method of claim 59 wherein the mammal is a human.

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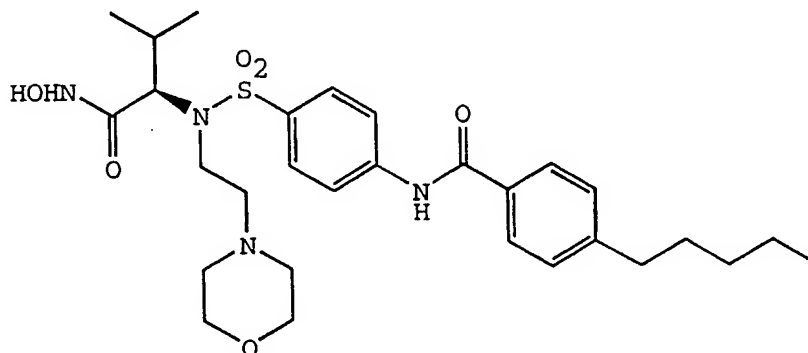
61. The method of claim 60 wherein the compound has the structure:



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or a salt, an enantiomer, a racemate, or a tautomer thereof.

62. The method of claim 60 wherein the compound has the structure:



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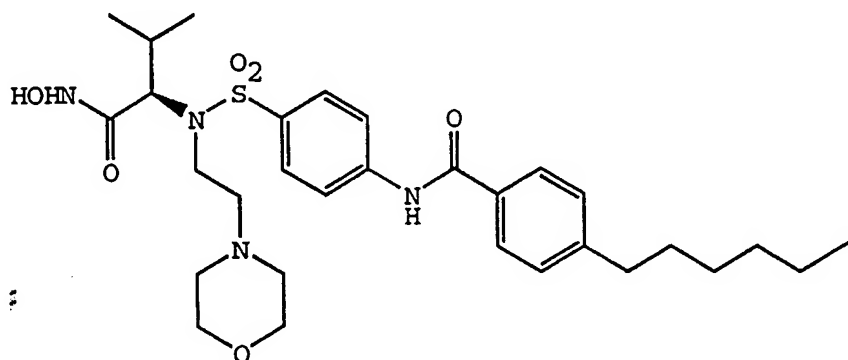
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or a salt, an enantiomer, a racemate, or a tautomer thereof.

63. The method of claim 60 wherein the compound has the structure:

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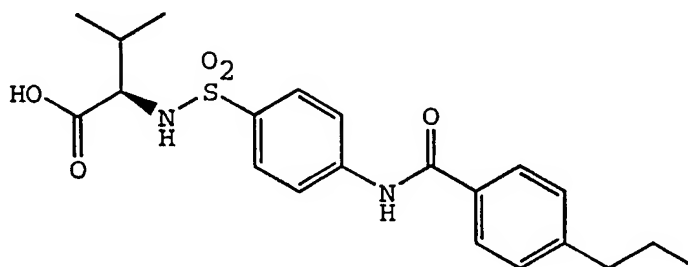


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or a salt, an enantiomer, a racemate, or a tautomer thereof.

64. The method of claim 60 wherein the compound has the structure:

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or a salt, an enantiomer, a racemate, or a tautomer thereof.

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